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10/626,159	07/24/2003	Vinod Sharma	P-11275.00	9695

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	**PAPER NUMBER**
1633	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/626,159	SHARMA, VINOD	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6 and 46-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6 and 46-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of an adenoviral associated vector as a species of a viral vector in the reply filed on 4/26/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Amended claims 1-3, 6 and new claims 46-56 are pending in the present application, and they are examined on the merits herein with the aforementioned elected species.

Response to Amendment

The rejection under 35 U.S.C. 101 because the claims encompass a non-statutory subject matter was withdrawn in light of Applicant's amendment.

The rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement was withdrawn upon further consideration and in light of the prior art applied below.

The rejection under 35 U.S.C. 102(e) as being anticipated by Donahue et al. (US 2002/0155101; IDS) was withdrawn in light of Applicant's amendment.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended claims 1-3, 6 and new claims 46-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. ***This is a modified rejection necessitated by Applicant's amendment.***

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

Applicant's invention is drawn to an implantable bio-ablation composition comprising a first coding sequence that **encodes and expresses in atrioventricular node cells**, **any molecule** that decreases expression of L-type Ca channels and thereby suppresses cellular excitability **and** a second coding sequence that encodes and expresses **any protein** that decreases the conductance of L-type Ca channels, whereby the expression of both the first and second sequences is effective to substantially extinguish conductance through the atrioventricular node.

However, apart from the specific disclosure of using **an exogenous polynucleotide encoding Kir/GEM** (GenBank accession number U13052) to decrease levels of L-type Ca channels in atrioventicular node cells and thereby decrease the cell

excitability (paragraph 0034); **an exogenous polynucleotide encoding Giα subunit** (GenBank accession number AH001470) to increase the dephosphorylation of the L-type Ca channel and thereby decreasing its conductance (paragraphs 0035-0036); and that the expression of L-type Ca channel can be suppressed through the use of **the dominant negative Ca(v)1.2 with an ascidian 3-domain type alpha 1 subunit** (paragraphs 0037 and 0072), the instant specification fails to describe relevant characteristics of a representative number of other species for **a broad genus** of a coding sequence that encodes and expresses in atrioventricular node cells a molecule that decreases expression of L-type Ca channels and thereby suppresses cellular excitability and a representative number of other species for **a broad genus** of a coding sequence that encodes and expresses a protein that decreases the conductance of L-type Ca channels in the bio-ablation composition as claimed.

The claimed invention as a whole is not adequately described. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure for a representative number of species for **a broad genus** of a coding sequence that encodes and expresses in atrioventricular node cells a molecule that decreases expression of L-type Ca channels and thereby suppresses cellular excitability and a representative number of species for **a broad genus** of a coding sequence that encodes and expresses a protein that

decreases the conductance of L-type Ca channels in the bio-ablation composition as claimed, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Response to Argument

Applicant's arguments related in part to the above rejection in the Amendment filed on 12/12/06 (pages 6-7) have been fully considered, but they are respectfully not found to be persuasive.

Applicant argues basically that amended claims recite a bio-ablation composition comprising a coding sequence that encodes and expresses a molecule that decreases expression of particular ion channels, namely, the L-type Ca channels, and further including a coding sequence that encodes and expresses a protein that decreases the conductance of L-type Ca channels. Additionally, newly added claims 51 and 56 further recite specific encoded proteins. Accordingly, the claims as amended recite nucleic

acid sequences that meet the Written Description requirement under 35 USC 112, first paragraph.

It is noted that apart from the disclosure of using **an exogenous polynucleotide encoding Kir/GEM** (GenBank accession number U13052) to decrease levels of L-type Ca channels in atrioventicular node cells and thereby decrease the cell excitability (paragraph 0034); and that the expression of L-type Ca channel can be suppressed through the use of **the dominant negative Ca(v)1.2 with an ascidian 3-domain type alpha 1 subunit** (paragraphs 0037 and 0072), what are the relevant or essential structural characteristics for other species within a broad genus of an encoded molecule that decreases directly and/or indirectly the expression of L-type Ca channels? Similarly, apart from the disclosure of using **an exogenous polynucleotide encoding Giα subunit** (GenBank accession number AH001470) to increase the dephosphorylation of the L-type Ca channel and thereby decreasing its conductance (paragraphs 0035-0036), what are the relevant or essential structural characteristics of other species within a broad genus of an encoded protein that decreases directly and/or indirectly the conductance of L-type Ca channels? Particularly, apart from the **Giα subunit** what are the structural characteristics possessed by any other Gi proteins having the same desired activity, namely decreasing the conductance of L-type Ca channels?

Please note that **one cannot describe what one has not conceived**. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

Accordingly, claims 1-3, 6 and 46-56 are rejected under 35 U.S.C. 112, first paragraph, for the lack of Written Description for the reasons set forth above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 6 and 46-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. ***This is a new ground of rejection necessitated by Applicant's amendment.***

The term "substantially extinguish" in independent claims 1 and 51 is a relative term which renders the claims indefinite. The term "substantially extinguish" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear to which degree a conduction through the atrioventricular node would be considered to be substantially extinguished, for example 1%, 5% or 10% relative to the normal conduction level. Therefore, the metes and bounds of the claims are not clearly determined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Amended claims 1-3, 6 and new claims 46-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Donahue et al. (US 2002/0155101; IDS) in view of Murata et al. (Circulation 106:19, abstract 36, 2002; IDS). ***This is a modified rejection necessitated by Applicant's amendment.***

Donahue et al. disclosed a composition comprising one or a combination of polynucleotides that encode the inhibitory Gαi2 subunit, G-protein subunit, connexin, gap junction protein and at least one ion channel protein including L-type Ca channel subunits having dominant negative activity, and others including genes for proteins that affect the expression, processing or function processing of the proteins affecting arrhythmias to cause a decrease in speed of conduction through at least the atrioventicular (AV) node (see at least the abstract; paragraphs 36-39, 44-53, 98 and 108). Donahue et al further teaches that a dominant negative protein has capacity to inactivate an endogenous protein (paragraphs 63-65), and that nucleic acid delivery systems including adeno-associated viral vector can be used (paragraph 71). Donahue et al disclosed by exemplification showing that over-expression of Gαi2 subunit is capable of decreasing speed of conductance through the atrioventricular node in an animal system as determined by standard electrophysiological assay (paragraphs 0101-0104, and examples).

Donahue et al does not teach specifically a composition further comprising a coding sequence coding for a molecule that decreases expression of L-type Ca channels, specifically a sequence encoding kir/GEM; even though the reference

teaches a composition to include polynucleotides encoding at least one ion channel protein including L-type calcium channel subunits having dominant negative activity, and others including genes for proteins that affect the expression, processing or function processing of the proteins affecting arrythmia.

At the effective filing date of the present application, Murata et al already disclosed a vector encoding kir/GEM and that exogenous expression of kir/GEM reduced L-type calcium current that mimics pharmacological calcium channel blockade in adult guinea pigs (see the abstract). Murata et al further disclosed that kir/GEM was previously demonstrated reduce calcium current by inhibiting alpha subunit trafficking of L-type calcium channels in PC12 cells (decreasing expression of L-type calcium channels).

It would have been obvious for an ordinary skilled artisan to modify the teachings of Donahue et al. by also incorporating a vector encoding kir/GEM in their composition to modulate the electrical property of the heart in an experimental model, particularly for decreasing the speed of conduction through at least the atrioventicular (AV) node in a mammal, in light of the teachings of Murata et al.

An ordinary skilled artisan would have been motivated to carry out the above modification because Murata et al already disclosed that exogenous expression of kir/GEM reduced L-type calcium current that mimics pharmacological calcium channel blockade in adult guinea pigs, and this is another approach that is resulting in inactivating the activity of endogenous L-type calcium channels.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Donahue et al., and Murata et al.; coupled with the high level of skill of an ordinary skilled artisan in the relevant art. The modified composition resulting from the combined teachings of Donahue et al. and Murata et al. is indistinguishable from the bio-ablation composition of the present application.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Argument

Applicant's arguments related in part to the above rejection in the Amendment filed on 12/12/06 (pages 13-14) have been fully considered, but they are respectfully not found to be persuasive.

Applicant argues that although Donahue discloses compositions that include a sequence encoding Gαi2, and Murata discloses compositions that include a sequence encoding kir/GEM, none of these references teaches or suggests or any motivation using the sequences together for any purpose, while the present amendment establishes that the plurality of sequences are included in a composition for the purpose of bio-ablation, and such an effect is neither taught nor suggested in neither Donahue nor Murata.

Firstly, please note that for a composition claim the intended use is not given any patentable weight. Nevertheless, Donahue et al. disclosed clearly a composition comprising one or a combination of polynucleotides that encode the inhibitory Gαi2

subunit, G-protein subunit, connexin, gap junction protein and at least one ion channel protein including L-type Ca channel subunits having dominant negative activity, and others including genes for proteins that affect the expression, processing or function processing of the proteins affecting arrhythmias **to cause a decrease in speed of conduction through at least the atrioventicular (AV) node** (see at least the abstract; paragraphs 36-39, 44-53, 98 and 108).

Secondly, an ordinary skilled artisan would have been motivated to carry out the modification set forth above because Murata et al already disclosed that exogenous expression of kir/GEM reduced L-type calcium current that mimics pharmacological calcium channel blockade in adult guinea pigs, and this is another approach that is resulting in inactivating the activity of endogenous L-type calcium channels, which Donahue et al also contemplated though the use of L-type Ca channel subunits having dominant negative activity to inactivate the endogenous protein.

Accordingly, claims 1-3, 6 and 46-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Donahue et al. (US 2002/0155101; IDS) in view of Murata et al. (Circulation 106:19, abstract 36, 2002; IDS) for the reasons set forth above.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Dave Nguyen, may be reached at (571) 272-0731.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system

provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

QUANG NGUYEN, PH.D.
PRIMARY EXAMINER